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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,919	10/20/2003	David B. Reitz		3966

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/689,919	REITZ ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE / MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08/26/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-110* is/are pending in the application.

4a) Of the above claim(s) *4-54,65-104 and 106-110* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3,55-64 and 105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This application is a continuation of SN10/151,211 and all claims stayed the same. Prosecution continues with the merit examination of the elected claims 61-64 and generic claims 1-3, 55-60, and 105 to the extend of the elected compounds.

A restriction was required in the parent case as following:

Group I, claim 6, drawn to alanine derivatives, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-5 and 105 readable on the elected subject matter of claim 6 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group II, claim 8, drawn to tyrosine derivatives, classified in class 568, subclass various, depending on species election. If this group is elected generic claims 1-5, 7 and 105 readable on the elected subject matter of claim 8 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group III, claim 11, drawn to glycine derivatives, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-5, 9-10 and 105 readable on the elected subject matter of claim 11 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group IV, claims 12-13, drawn to indolyl derivatives, classified in class 548, subclass various, depending on species election. If this group is elected generic claims 1-5 and 105 readable on the elected subject matter of claims 12-13 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group V, claims 14-17, drawn to nonheterocyclic inhibitors, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-5 and 105 readable on the elected subject matter of claims 14-17 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group VI, claims 25, drawn to dopa derivatives, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, 18-24 and 105 readable on the elected subject matter of claim 25 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group VII, claim 31, drawn to ethanonaphthanyl compounds, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, 26-30 and 105 readable on the elected subject matter of claim 31 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group VIII, claim 32, draw to acids, classified in class 560, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claim 32 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group IX, claims 33-37, drawn to propionic acid derivatives, classified in class 560, subclass various, depending on species election. If this group is elected generic claims 1-3 and 105 readable on the elected subject matter of claims 33-37 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group X, claim 38, drawn to heterocyclic inhibitors, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claim 38 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XI, claims 45-46, drawn to unsaturated inhibitors, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, 39-44 and 105 readable on the elected subject matter of claim 45-46 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XII, claim 55, drawn to picolinates, classified in class 546, subclass various, depending on species election. If this group is elected generic claims 1-3, 47-54 and 105 readable on the elected subject matter of claim 55 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XIII, claim 61-64, drawn to pyridinyl compounds, classified in class 546, subclass various, depending on species election. If this group is elected generic claims 1-3, 56-60 and 105 readable on the elected subject matter of claim 61-64 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XIV, claims 65-69, drawn to dopamine hydroxylase inhibitors, classified in class 546-548, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claim 65-69 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XV, claims 70-72, drawn to imidazoles, classified in class 548, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claims 70-72 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XVI, claim 88, drawn to conjugates, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, 73-87 and 105 readable on the elected subject matter of claim 88 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XVII, claims 89-92, drawn to tyrosine hydroxylase inhibitors, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claim 89-92 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XVIII, claims 93-96, drawn to dopadecarboxylase inhibitors, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claims 93-96 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XIX, claims 97-104, drawn to dopadecarboxylase inhibitors, classified in class various, subclass various, depending on species election. If this group is elected generic claims 1-3, and 105 readable on the elected subject matter of claims 97-104 will be prosecuted together with the election. A further election of a single disclosed species is also required.

Group XX, claim 107, drawn to method of treating chronic hypertension, classified in class 514, subclass various, depending on species election. If this group is elected a further election of a single disclosed species to be used for the method is also required.

Group XXI, claim 108, drawn to method of treating congestive heart failure, classified in class 514, subclass various, depending on species election. If this group is elected a further election of a single disclosed species to be used for the method is also required.

Group XXII, claim 109, drawn to method of treating cirrhosis, classified in class 514, subclass various, depending on species election. If this group is elected a further election of a single disclosed species to be used for the method is also required.

Group XXIII, claim 110, drawn to method of treating nephrosis, classified in class 514, subclass various, depending on species election. If this group is elected a further election of a single disclosed species to be used for the method is also required.

Group XXIV, claim 106, drawn to method of treating sodium retention (not encompassed by claims 109-110), classified in class 514, subclass various, depending on species election. If this group is elected a further election of a single disclosed species to be used for the method is also required.

The above groups are independent and patentably distinct inventions because each group of compounds differ in structure to such an extend that a reference anticipating any one group of compounds would not render another group obvious. The search for each structurally distinct group of compounds are not coextensive. Each method of treating a distinct disease is distinct because the active ingredients, dosage, site of administration and mechanism of treatment is specific and distinct for each disease.

Applicants argued that all the groups are conjugates of a synthetic inhibitor component, a cleavable carrier component and a linker component is not persuasive since no documentation to show that the above structurally distinct products are obvious variants of each other.

Should applicant traverse on the ground that the above groups are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the groups to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention. In the instant case then there could have been no patentability over Hans Bundgaard p.188 since the dopa conjugates anticipates group VI products.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Since this application is a continuation of SN 10/151,211 which is a continuation of SN 09/678,015 which is a continuation of 09/444,888 which is a continuation of SN 08/639,493 which is a continuation of SN 08/280,170 and all claims stayed the same, prosecution continues with the merit examination of claims 61-64 and generic claims 1-3, 56-60 and 105 to the extend of the elected compounds. Claims 4-54,65-104 and 106-110 are withdrawn from consideration per 37 CFR 1.142(b).

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 55-59, 61-62 and 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Stanton et al. US 4,678,800.

See col. 19-20 conjugates of examples 9 and 12, meet the claimed requirement wherein the first and second residues forms cleavable bonding between amino and carboxyl groups of the residues (base claims 2-3) and the first residue is a pyridinyl compound of claims 61 or 62.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 55-64 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Umezawa BE757336, or Kuhnis et al US 3,998,955 or Banyu Pharm. GB 1,453,673 in view of Bundgaard or Lee (Clin. Ex. Practice) and Fuhrer et al. EP 139917 or Hofbauer J. Pharm. Ther. or Nievelstein et al. CA 104.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Determination of the scope and content of the prior art (MPEP §2141.01)

Umezawa '336 or Kuhnis '955 or Banyu '673 disclosed the different substituted picolinic acid and its amide or amido-carbonyl compounds as antihypertensive agents.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The disclosure of Umezawa '336 and Kuhnis '955 or Banyu '673 containing all the elements of the claims **except** the prior art disclosed the active compounds while the instant claims are drawn to the prodrug conjugates for these conventional antihypertensive compounds for the same utility.

Bundgaard and Lee taught that prodrug preparation is conventional pharmaceutical formulation for administering of a biological active agents to the active site. Fuhrer '917 is an alternative prodrug preparation which have antihypertensive activity. Specifically, the γ-glutamyl prodrug conjugate is well recognized for its renal tubular specific purpose (see Bundgaard p.188 second paragraph).

Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be motivated to prepare formulation of picolinic acid employing the conventional prodrug formation because of its suggested advantage in better targeting to the active site. Furthermore, in analogous antihypertensive agents (see Hofbauer or Nieveslstein), prodrug preparation using N-acetylglutamyl conjugation resulted in better hemodynamics for sodium excretion which is desirable for such drug.
In view of the disadvantage of picolinic acid having local irritation (see BE'336 abst), one having ordinary skill in the art would be motivated to prepare the conventional antihypertensive picolinic compounds using the well taught conventional prodrug skill choosing the γ-glutamyl conjugate since such particular prodrug was suggested to have the added advantage of further increasing sodium excretion.

4. This is a continuation of applicant's earlier Application No. 10/151,211 which is a continuation of SN 09/678,015 which is a continuation of 09/444,888 which is a continuation of SN 08/639,493 which is a continuation of SN 08/280,170 and all claims are drawn to the same invention claimed in the earlier applications and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

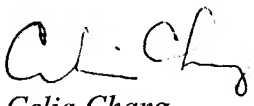
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane, can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



OACS/Chang
May 10, 2004

Celia Chang
Primary Examiner
Art Unit 1625